

Definition

We measure serum total CO₂ content in lieu of measuring serum bicarbonate. The total CO₂ content includes the serum bicarbonate as well as available forms of carbon dioxide (i.e., dissolved CO₂ and carbonic acid). Generally, the serum bicarbonate comprises about 95% of the total CO₂ content; thus we can use this measurement as an excellent estimator of serum bicarbonate. The total CO₂ content normally equals 23 to 30 mEq/L of serum.

Technique

Most laboratories use an autoanalyzer for measuring total CO₂ content. This method measures the amount of CO₂ liberated from the sample after adding a strong acid. The CO₂ diffuses across a dialysis membrane. A bicarbonate-carbonate buffer solution containing an indicator dye absorbs the CO₂. A colorimeter then evaluates the new color, which it converts to a total CO₂ measurement.

Two potential problems exist with this method: (1) the color reagent may change with time, thus the laboratory must frequently check standardization curves; (2) exposure of the sample to air will allow loss of CO₂, as much as 6 mEq/L in an hour.

Arterial blood gas reports generally include a bicarbonate value. The blood gas machine measures pH and pCO₂ and then calculates a bicarbonate value using the Henderson-Hasselbalch equation. Generally, a concurrent venous total CO₂ content will exceed this value by less than 2 to 4 mEq/L, of which 1 to 2 mEq/L represents the difference between venous and arterial blood; the remaining difference comes from dissolved CO₂.

Basic Science

The kidneys and lungs maintain daily acid-base balance. Understanding this normal physiology allows us to appreciate abnormalities. This discussion refers to bicarbonate rather than total CO₂ content, as we measure total CO₂ content as a surrogate for bicarbonate.

Bicarbonate and carbonic acid constitute the major buffer pair in body fluids. Carbonic acid dissociates into hydrogen ion and bicarbonate with a dissociation constant of 7.95×10^{-7} . Carbonic acid also maintains an equilibrium with H₂O and CO₂.



We usually describe dissociation constants and hydrogen ion concentrations as negative logarithms. Thus, the negative logarithm of the dissociation constant equals 6.1. This value is called the pK_a. Normal hydrogen ion concentration

equals 40 nanoequivalents/liter, corresponding to a pH of 7.4.

The familiar Henderson-Hasselbalch equation derives from these facts:

$$\text{pH} = 6.1 + \log \frac{[\text{HCO}_3^-]}{[\text{H}_2\text{CO}_3]}$$

Carbonic acid concentration is proportional to the partial pressure of carbon dioxide (pCO₂) in the blood. Multiplying the pCO₂ by a constant (0.03) estimates the carbonic acid concentration, giving the useful form of the above equation:

$$\text{pH} = 6.1 + \log \frac{\text{HCO}_3^-}{0.03 \times \text{pCO}_2}$$

Changes in hydrogen ion concentration (pH) result from changes in either bicarbonate or carbon dioxide. Measurement of total CO₂ content can help us explain acid-base disorders (when the pH and pCO₂ are known). Furthermore, since we often measure total CO₂ content as part of automated chemistry determinations, this measurement can provide the first clue to acid-base disturbances.

We produce approximately 1 mEq/kg daily of hydrogen ions (derived from metabolism of proteins primarily). The kidney normally excretes this daily acid load. Failure of excretion forces the reaction of H⁺ and HCO₃⁻, resulting in a decrease of bicarbonate concentration.

Bicarbonate reabsorption occurs primarily in the proximal tubule. Carbonic anhydrase controls this absorption. The patient's volume status has a major influence on absorption, since sodium is reabsorbed along with this bicarbonate. Thus, volume contraction stimulates both sodium and bicarbonate reabsorption. This results in an increased total CO₂ content. Likewise, volume expansion can lead to a mild decrease in total CO₂ content.

Hydrogen ion concentration (pH) is another major determinant of bicarbonate reabsorption. Thus, the kidney will respond to changes in ventilation (pCO₂) with compensatory changes in bicarbonate reabsorption. For example, chronic hypoventilation (↑ pCO₂) causes a decreased pH. This decreased pH stimulates bicarbonate reabsorption, thus the patient will have an increased total CO₂ content.

Clinical Significance

The major caveat concerning total CO₂ content involves the interpretation of an isolated measurement. *One cannot diagnose acid-base disturbances from an isolated total CO₂ measurement.* In order to characterize an acid-base disturbance, one needs pH, pCO₂, total CO₂, as well as a measurement of the anion gap. Given that caveat, one can use the following guidelines.

Table 196.1
Causes of Increased Anion Gap Metabolic Acidosis

Lactic acidosis
Ketoacidosis
 Diabetic
 Starvation
 Alcoholic
Poisonings
 Methanol
 Ethylene glycol
 Paraldehyde
 Salicylates
Renal failure

Table 196.2
Causes of Normal Anion Gap (Hyperchloremic)
Metabolic Acidosis

Diarrhea
Acetazolamide (Diamox)
Urinary tract—bowel connections
Ileal conduit
Renal tubular acidoses
 Type I—distal
 Type II—proximal
 Type IV—hypoaldosterone
 Moderate renal failure
Dilutional acidosis
Acid administration
 HCl
 Hyperalimentation
 Lysine or arginine chloride

Low levels of total CO_2 result from either metabolic acidosis or as a compensation to respiratory alkalosis. Bicarbonate levels below 10 mEq/L virtually identify metabolic acidosis as the cause, as compensation for respiratory alkalosis will not drive the bicarbonate that low.

If metabolic acidosis is present, one should distinguish between increased anion gap and nonanion gap acidosis. The simplest formula for the anion gap is:

$$\text{AG} = \text{Na}^+ - (\text{HCO}_3^- + \text{Cl}^-)$$

$$\text{nl} \approx 4\text{--}12 \text{ mEq/L}$$

Table 196.1 lists the differential of an anion gap acidosis. Generally, one does not consider this differential until the

Table 196.3
Causes of Metabolic Alkalosis

Vomiting
Diuretic therapy
Excess mineralocorticoids
 Hyperaldosteronism
 Cushing's syndrome
 Bartter's syndrome
 Licorice ingestion
Hypokalemia
Posthypercapnic
Volume contraction

gap exceeds 20 mEq/L. Table 196.2 gives the differential for nonanion gap acidosis.

Similar to the interpretation of a decreased bicarbonate level, an increased bicarbonate level may result from either a metabolic alkalosis or as compensation to respiratory acidosis. Table 196.3 lists the causes of metabolic alkalosis.

In summary, the serum total CO_2 content can give clues to acid-base abnormalities. When used in conjunction with the pH and pCO_2 , this measurement helps us define possible causes of metabolic imbalance, especially in acutely ill patients.

References

- Bia M, Thier SO. Mixed acid-base disturbances: a clinical approach. *Med Clin North Am* 1981;65:347-61.
- Emmett ME, Narins RG. Clinical use of the anion gap. *Medicine* 1977;56:38-54.
- Gabow PA, Kaehny WD, Fennessey PV, et al. Diagnostic importance of an increased serum anion gap. *N Engl J Med* 1980;303:854-58.
- Kassirer JP. Serious acid-base disorders. *N Engl J Med* 1974;291:773-76.
- Narins RG, Emmett M. Simple and mixed acid-base disorders: a practical approach. *Medicine* 1980;59:161-87.
- Narins RG, Gardner LB. Simple acid-base disturbances. *Med Clin North Am* 1981;65:321-46.
- Oh MS, Carroll HJ. The anion gap. *N Engl J Med* 1977;297:814-17.
- Seldin DW, Rector FC. The generation and maintenance of metabolic alkalosis. *Kidney Int* 1972;1:306-21.